DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the arguments/amendments filed on 11/29/2011 wherein claim 27 has been amended.

2. Claims 1-20 and 26-32 are presented for examination on the merits. The following rejections are made.

Response to Applicants' Arguments

3. Applicants arguments filed 11/29/2011 regarding the rejection of claims 1-19 and 26-31 made by the Examiner under 35 USC 103(a) over Struengmann et al. (US 6284269) in view of Bock et al. (US 6869948) and Robinson et al. (US 6071539) have been fully considered but they are not found persuasive and is **MAINTAINED** for the reasons of record in the office action mailed on 8/1/2011.

4. In regards to the 103(a) rejection, Applicant asserts the following:

A) There is no motivation cited by the Examiner to modify the tablet of Struengmann; and

B) the skilled person in the art would need to change almost all components of the prior art to achieve the claimed invention. Such radical alterations are not within the realm of obvious substitutions as the office asserts.

5. In response to A, Applicants arguments are not found persuasive. With respect to modifying the tablet of Struengmann, the Examiner maintains their position that the modifications made thereto are obvious. First, with respect to Struengmann being in the form of a tablet, it is noted that these tablets are comprised of compressed granules/particles. Based from all of the examples of Struengmann, the tablet ingredients are mixed together, granulated and the

resulting granules are compressed together forming tablets. Thus, while Struengmann teaches tablets as a dosage form, those tablets are comprised of compressed water soluble meloxicam granules. While the Examiner does point to Bock using granules themselves (without their tabletting) as an accepted dosage form, Bock's significance is their teaching that meglumine is employed to improve the solubility of meloxicam which in turn would improve meloxicam's bioavailability and consequently its ability to treat pain.

6. In response to B, the Examiner is not making any radical alterations. The only major alteration suggested is that of using the meglumine salt of meloxicam in the formulation of Struengmann at a ratio of 1.2:1 to 1:1.2 (meglumine to meloxicam). Again, as was noted above, the meglumine salt of meloxicam improves the drugs water solubility so one would have had sufficient motivation to use it.

7. Applicants arguments filed 11/29/2011 regarding the rejection of claims 20 and 32 made by the Examiner under 35 USC 103(a) over Struengmann et al. (US 6284269) in view of Bock et al. (US 6869948) and Ouali (US 6183779) have been fully considered but they are not persuasive and is **MAINTAINED** for the reasons of record in the office action mailed on 8/1/2011.

8. In regards to the 103(a) rejection, Applicant asserts the following:

C) Merely because the office asserts that a component such as glucose is known to exist does not make its combination with meloxicam and the other claimed components obvious.

9. In response to C, Applicant is claiming a very generic formula comprising commonly used excipients. Ouali is cited for their teaching of commonly employed excipients in their pharmaceutical granules. It is the position of the Examiner that it is not inventive to formulate a

composition that includes a well known active agent associated with other well known pharmaceutical excipients. For instance, Ouali teaches that glucose, povidone and HPMC are commonly used for their binding ability in granular composition, so if one combined them together to the meloxicam granule of Struengmann, the result would be a particle with sufficient binding strength to retain the meloxicam within the dosage form and ensure its administration to the end user. Applicants formula is generic and is obvious, especially absent any evidence showing a truly unexpected or surprising effect.

Maintained Rejections, of Record
Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. **Claims 1-19 and 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Struengmann et al. (US 6284269; published 9/4/2001) in view of Bock et al. (US**

6869948; filed 3/26/1999, of record) and Robinson et al. (US 6071539; published 6/6/2000, of record).

13. Struengmann is directed to fast disintegrating meloxicam formulations. Example V/9 teaches a tablet (with total weight of 3142 mg) comprising meloxicam (58 mg), lactose (1102 mg) (water soluble carrier), polyvinylpyrrolidone (37.7 mg) (water soluble binder), citric acid (942.5 mg) (water soluble carrier), sodium hydrogen carbonate (333.5 mg) (water soluble carrier), sodium sulfate (348 mg) (water soluble carrier), saccharin (8.7 mg) (sweetener), aspartame (58 mg) (sweetener) and flavoring agents. The total weight percent of meloxicam is about 1.8% by weight, the carrier is present in the formulation is about 87% by weight, the sweetener is present in an amount of about 2.4% by weight and the binder is present in an amount of about 1.2% by weight (math not shown: designations above used). It's noted that Example V/9 includes polydimethylsiloxane which is hydrophilic yet insoluble, however as it is present in an amount of 0.4% by weight, it would be expected to not impact the water solubility of the formulation.

14. Struengmann fails to teach the meloxicam as being present as a meglumine salt. Struengmann also fails to teach the flavorant as being selected from the group consisting of vanilla, honey, apple or contramarum.

15. Bock is directed to oral meloxicam compositions. Granular formulations are disclosed in Examples 6 and 7. It is taught that the meloxicam may be a sodium or megluine salt (see claim 1) in order to improve drug (meloxicam) solubility. The ratio between meglumine and meloxicam is taught to be from 1.2:1 to 1:1.2 (see instant claims 18 and 19).The concentration of meloxicam in the granules is about 2% (see Example 6) and 3.5% by weight (see Example 7; see

instant claim 17). Moreover, Bock teaches employing the carrier agent(s) (lactose and microcrystalline cellulose) in an amount of about 91% (see Example 6) and 72% (see Example 7). Thus, while Struengmann teaches tablets as carriers for meloxicam, one would have envisaged granules as well as a suitable means for providing analgesic relief to a user in need thereof. Moreover, one would have been motivated to employ meglumine as its presence greatly enhances water solubility of the meloxicam.

16. Robinson is directed to effervescent granules. The granules may be used to provide analgesic relief to a user thereof. The granules are to comprise taste-masking agents such as sweeteners like aspartame. Table 3 provides a tablet formed from granular particles. The granular particles comprise 5% by weight of aspartame (sweetener) (see column 20, lines 30-40). Flavorants included may be either vanilla or apple.

17. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the formulation of Struengmann with the meglumine of Bock and the apple and/or vanilla flavorant of Robinson a reasonable expectation for success in arriving at a water soluble meloxicam granule comprising meloxicam, a salt forming agent such as meglumine, a binder, a sugar, a carrier and optionally flavorants and other excipients. With respect to the recitation by Applicant that the 5 grams of the instant granules dissolve in 100 mL in demineralized water in about 1 minute to form a clear solution, this would be a property of the obvious composition. As the obvious formulation comprises meloxicam, a salt, a binder, a sugar and a carrier as is instantly claimed, it would be expected to have the properties as instantly claimed, absent evidence to the contrary. With respect to the amounts of binder, sweetener and carrier present in the invention, these are obvious as well. Struengmann teaches including a

binder in an amount of about 1.2% and a carrier in an amount of 87% by weight and Robinson teaches providing a sweetener (aspartame) in an amount of 5% by weight. While the binder concentration is less than 2%, Applicants use of "about 2 to about 8 percent" encompasses values reasonably below 2%. Thus, 1.2% is obvious over "about 2%" as an ordinarily skilled person would reasonably recognize that 1.2 is encompassed in the relative amount of about 2%. Therefore, a water soluble granule comprising meloxicam, a salt forming agent, a binder, a carrier, a sweetener and an optional flavorant is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

18. With respect to claims 27-30, Applicant has failed to define what compounds materially affect the basic and novel characteristics of the claimed invention. As Applicant has failed to provide a clear indication for 'consisting essentially of', 'consisting essentially of' will be construed as equivalent to 'comprising', and thus are included in the above rejection. See MPEP 2111.03.

19. **Claims 20 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Struengmann et al. (US 6284269; published 9/4/2001) in view of Bock et al. (US 6869948; filed 3/26/1999, of record) and Ouali).**

20. Struengmann and Bock are discussed in detail above. Briefly, they together teach a composition comprising meglumine, meloxicam and soluble povidone.

21. Struengmann and Bock fail to teach a composition comprising (and consisting essentially) of meloxicam, meglumine, hydroxypropylmethylcellulose (HPMC), soluble povidone and glucose monohydrate.

22. Ouali is directed to stabilizer pharmaceutical composition of a NSAID and a prostaglandin. The composition may be in the form of a granule. The NSAID containing area is to comprise various excipients such as binders and fillers/carriers. Exemplified binders include, but are not limited to, starch (including corn starch and pregelatinized starch), gelatin, sugars (including sucrose, glucose, dextrose and lactose), polyethylene glycol, waxes, and natural and synthetic gums, e.g., acacia sodium alginate, polyvinylpyrrolidone, cellulosic polymers (including hydroxypropyl cellulose, hydroxypropyl methylcellulose, methyl cellulose, hydroxyethyl cellulose, and the like), and Veegum. Exemplified carriers/fillers include, for example, insoluble materials such as silicon dioxide, titanium oxide, alumina, talc, kaolin, powdered cellulose, microcrystalline cellulose, and the like, as well as soluble materials such as mannitol, urea, sucrose, lactose, dextrose, sodium chloride, sorbitol, and the like (see column 5, line 50 to column 6, line 10). Thus, as it is known that glucose and HPMC are known binders, it would be obvious to employ them in the granule of Struengmann and Bock with a reasonable expectation in imparting suitable binding and/or carrier benefit to the granule formulation.

23. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the formulation of Struengmann with the meglumine of Bock and excipients such as glucose and HPMC as taught by Robinson with a reasonable expectation for success in arriving at a water soluble granule comprising meloxicam, meglumine, HPMC, povidone and glucose. While Ouali fails to teach the glucose as being present as glucose monohydrate, it's well known (common knowledge) that glucose is generally in the form of a monohydrate. With respect to the combining HPMC and glucose of Ouali with dosage form of Streungmann and Bock, this is obvious. Ouali is cited as a general reference for their teaching of

excipients commonly used in the delivery of NSAID actives. Knowing that povidone, HPMC and glucose may be employed as binders in pharmaceutical formulations, it would have been obvious to use them together in a combination to deliver meloxicam with a reasonable expectation for success in providing analgesic benefit to a user thereof. Therefore, the instantly claimed subject matter is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

24. With respect to claim 32, Applicant has failed to define what compounds materially affect the basic and novel characteristics of the claimed invention. As Applicant has failed to provide a clear indication for 'consisting essentially of', 'consisting essentially of' will be construed as equivalent to 'comprising'. See MPEP 2111.03.

Conclusion

25. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

26. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

29. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/K Purdy/
Examiner, Art Unit 1611
February 23, 2012

/Allison M. Ford/
Primary Examiner, Art Unit 1653